REMARKS

Claims 15-26 are pending in the application. Claim 15 is an independent claim.

Claims 15-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite. Claims 16-26 depend from claim 15.

It is proposed that Claim 15 be amended to recite that the conjugate is impregnated in a matrix material. Support for the amendment is found in the specification and particularly at page 9 lines 4-5. It is further proposed that Claim 15 be amended in accordance with the Examiner's suggestion, adding also that the second label is a direct visually detectable label. Support for the amendment is found in the specification at page 2, second paragraph; page 3, last paragraph; and page 11, fourth paragraph. No new matter is added by virtue of the amendments. The amendments to the claims are properly entered here since they do not raise any issues requiring additional search and they either put the claims in condition for allowance or at least in a better form for appeal. Entry of the proposed amendments is requested.

The claims are believed to be sufficiently definite for purposes of 35 U.S.C. 112, second paragraph. Accordingly, reconsideration of the rejection leading to its withdrawal is respectfully requested.

Claims 15-17 and 20-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fitzpatrick et al (US 5,451,504) in view of Decker et al. (US 4,230,683). The rejection proffers that it would have been obvious . . . to modify the device of Fitzpatrick et al. by using the hapten-labeled method of Decker et al.

The element of the present invention uses a first conjugate and a universal conjugate in an element for the determination of an analyte. The first conjugate comprises a low molecular organic molecule as a first detectable label and a bioaffine binding partner capable of a specific binding reaction with the analyte to be determined. The universal conjugate is a stable conjugate comprising a direct visually detectable label and a

bioaffine binding partner that has a high sensitivity towards a low molecular organic molecule.

It is submitted that the resulting combination or modification proffered by the rejection fails to show or suggest the claimed invention in light of the amendments. In that regard, it is submitted that the element of the present invention greatly reduces the need for optimization work especially with regard to the storage life of the components on the element and the sensitivity of these components. This optimization work is reduced mainly due to the components of the first conjugate, which due to their nature, can be much more simply optimized than can be a conjugate composed of a bioaffine binding partner that varies according to the analyte and a visually detectable label, which are often both very heterogeneous and cannot be determined exactly and thus with reference to the product are difficult to produce in the same reproducible quality.

It is submitted that Fitzpatrick et al. fails to disclose or suggest an element with two conjugates as recited in claim 15 and in fact, teaches away from such an element. Fitzpatrick et al. discloses at most a device with a mobilizeable receptor capable of binding an analyte, wherein a receptor-analyte complex is detected by observing a signal from a label attached to the receptor.

In order to highlight the differences between the claimed element and the device of Fitzpatrick et al., the Examiner's attention is first directed to the list of suitable detectable labels of Fitzpatrick et al. at Column 8 lines 33-38. Several of the suitable detectable labels, including that of the preferred embodiment (Col. 8 lines 38-40), which are attached to the receptor of the receptor-analyte complex, have intrinsic color such as dyes, colloidal gold, and latex particles. This is in direct contrast to the element of the present invention, wherein the conjugate that binds analyte has a low molecular organic molecule as its label.

Applicants' ignored this teaching of Fitzpatrick as they recognized and taught in the specification at page 2, second paragraph, that when direct labels are used with a

bioaffine binding partner that varies according to the analyte, optimal conditions have to be created on the analytical element for reaction and storage. This individual adaptation to the analyte to be determined is very laborious. Difficulties include stability and varying spatial arrangements that can lead to steric problems when such conjugates are reacted with the analyte and can thus result in poor sensitivity. The present invention overcomes these disadvantages by providing an element that comprises two bioaffine binding partners. The partner that is capable of a specific binding reaction with the analyte to be determined is part of a conjugate with a low molecular organic molecule detectable label. As such, the preferred embodiment of Fitzpatrick (Column 8 lines 38-41) not only fails to teach the element of the present claims, but works to lead one skilled in the art away from it.

Differences between the claimed element and the device of Fitzpatrick et al. also exist by Fitzpatrick et al. teaching of non-visible detectable labels. Fitzpatrick et al. at most teaches that these enzymes, fluorophores, chromophores, radioisotopes, and chemiluminescent agents, which are used to detect the receptor-analyte complex, are bound directly to its receptor-analyte complex. Such a complex is in direct contrast to the element of the present invention that comprises a universal conjugate that has "a second bioaffine binding partner and a second detectable label, the second bioaffine binding partner is capable of a specific binding reaction with the first detectable label, wherein the second detectable label is a direct visually detectable label".

Applicants' also ignored this teaching of Fitzpatrick as they recognized and taught in the specification at page 2, first paragraph that it is undesirable to use detectable labels that are not visible because additional measures have to be taken and furthermore may result in technical difficulties. The present invention overcomes this disadvantage by providing a stable conjugate composed of a direct visually detectable label and a bioaffine binding partner which has a high sensitivity towards the low molecular organic molecule of the conjugate. As such, the additional examples of suitable detectable labels of Fitzpatrick (Column 8 lines 32-35) not only fail to teach the element of the present claims, but work to lead one skilled in the art away from the element of the present invention.

It is respectfully submitted that the secondary reference to Decker et al. fails to cure the above-stated inadequacies of Fitzpatrick et al. In this regard the Examiner's attention is directed to Column 2 lines 43-44, which discloses the use of labeled antibodies (^{125}I, enzymes, and fluorescent chemicals). Decker et al. is devoid of description or suggestion of a direct visually detectable label, let alone a universal conjugate that comprises a second bioaffine binding partner and a direct visually detectable label, wherein the second bioaffine binding partner is capable of a specific binding reaction with a first detectable label of the conjugate capable of a specific binding reaction with the analyte to be determined.

The combination of Fitzpatrick et al. and Decker et al. cannot be motivated by hindsight in view of Applicants' specification. There is no motivation in the cited references to replace the binding partner for the analyte that is labeled with a direct visually detectable label as taught by Fitzpatrick et al. by the rather complex system of Decker et al., which does not encompass such direct visually detectable labels. It is submitted that the combination of the teachings of Fitzpatrick et al. and Decker et al. would lead to a system in which a binding partner for the analyte is labeled with a low molecular organic molecule that can be bound by another binding partner for this low molecular organic molecule that in turn carries a label that is not directly visually detectable. This is clearly not what is claimed in the presently amended claim 15.

Moreover, it is submitted that Decker et al. requires that its test sample be bound to a solid support. See, for example, Col. 1 lines 56-63, Col. 2 lines 4-10 and 59-66, and Col. 3 lines 28-32 where an assay for determining antigen or antibody from a test sample bound to a solid support is taught.

In light of the above, it is submitted that Fitzpatrick et al. and Decker et al. when taken as a whole, fail either alone or in combination to disclose or suggest an element comprising "a sample application zone, a detection zone . . . a zone containing immobilized analyte or analyte analogue . . . a material that enables liquid transport between the zones, a conjugate impregnated in a matrix material located upstream of the zone containing

immobilized analyte or analyte analogue, the conjugate can be detached from the matrix material by liquid and comprises a first bioaffine binding partner capable of a specific binding reaction with the analyte to be determined and a first detectable label, wherein the first detectable label is a low molecular organic molecule, and a universal conjugate, located upstream of the zone containing immobilized analyte or analyte analogue, which can be detached by liquid and comprises a second bioaffine binding partner and a second detectable label, the second bioaffine binding partner is capable of a specific binding reaction with the first detectable label, wherein the second detectable label is a direct visually detectable label", as required by amended claim 15. Claims 16-17 and 20-23 depend from claim 15.

It is respectfully submitted that the differences between the claimed invention and the cited art are such that Applicant's invention as a whole would not have been obvious to one of ordinary skill in the art at the time the invention was made. It is respectfully contended that the claimed invention meets the test of patentability under 35 U.S.C. 103(a). Reconsideration of the rejection of the claims and withdrawal of the rejection is respectfully requested.

Claims 18, 19, and 24-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fitzpatrick et al. in view of Decker et al. as applied to claims 15-17 and 20-23 above, and further in view of Bernstein et al (US 5,824,268). Fitzpatrick et al. and Decker et al. have been discussed above with reference to independent claim 15. As discussed above, it is submitted that neither Fitzpatrick et al. nor Decker et al. either alone or in combination with one another disclose or suggest the element of claim 15. Claims 18, 19 and 24-26 depend from independent claim 15.

Bernstein et al. discloses a test strip having three zones – a reaction zone, a sample zone, and a detection zone. Bernstein et al. fails to cure the inadequacies of Fitzpatrick et al. and Decker. It is therefore respectfully submitted that Bernstein cannot be said to provide suggestion or motivation to modify Fitzpatrick et al. and Decker et al. to meet the requirements of dependent claims 18, 19, and 24-26.

Accordingly, it is submitted that the claimed invention meets the test of patentability under 35 U.S.C. 103(a). Reconsideration of the rejection of the claims and withdrawal of the rejection is respectfully requested. The claims as submitted herein are believed to be in condition for allowance, and allowance of the application is respectfully requested. In addition, it is requested that any fees due be charged to Deposit Account Number 50-0877 with reference to (BMID 9941 US).

Respectfully submitted,

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Jill L. Woodburn, Reg. No. 39,874
The Law Office of Jill L. Woodburn, L.L.C.
128 Shore Drive
Ogden Dunes, IN 46368-1015
Telephone No.: 219-764-4005
Facsimile No.: 219-764-4070